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Supplementary file

Table S1. Search strategy.

MEDLINE (Ovid)
1. exp peptic ulcer/
2. exp peptic ulcer hemorrhage/
3. (pep$ adj5 ulcer$).tw.
4. (stomach adj5 ulcer$).tw.
5. (duoden$ adj5 ulcer$).tw.
6. (gastr$ adj5 ulcer$).tw.
7. exp gastritis/
8. gastritis.tw.
9. gastropathy.tw.
10. (bleed$ adj5 ulcer$).tw.
11. (rebleed$ adj5 ulcer$).tw.
12. (gastrointestinal adj5 bleed$).tw.
13. (gastrointestinal adj5 rebleed$).tw.
14. (gastrointestinal adj5 hemorrhag$).tw.
15. (gastrointestinal adj5 haemorrhag$).tw.
16. (ulcer adj5 hemorrhag$).tw.
17. (ulcer adj5 haemorrhag$).tw.
18. (mucos$ adj5 injur$).tw.
19. exp pyloric stenosis/
20. (pylor$ adj3 stenosis).tw. or (obstruct$).tw.
21. (gastrointestinal adj3 perforat$).tw.
22. (gi adj3 perforat$).tw.
23. (ulcer$ adj3 perforat$).tw.
24. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25. exp Anti-inflammatory agents, non-steroidal/
26. nsaid$.tw.
27. nonsteroid$ anti-inflammator$.tw.
28. non-steroid$ anti-inflammator$.tw.
29. nonsteroid$ antiinflammator$.tw.
30. non-steroid$ antiinflammator$.tw.
31. (naproxen or diclofenac or piroxicam or tenoxicam or Ibuprofen or etodolac or nabumetone or flurbiprofen or ketoprofen or tiaprofenic or pisoxica or piroxen or sulindac or tolmetin or indomethacin or loxoprofen or diflunisal or meloxicam or nimesulide).tw.
32. 25 or 26 or 27 or 28 or 29 or 30 or 31
33. exp cyclooxygenase 2 Inhibitors/
34. (celecoxib or etoricoxib or lumiracoxib or rofecoxib or valdecoxib or parecoxib).tw.
35. 33 or 34
36. randomized controlled trial.pt.
37. controlled clinical trial.pt.

38. randomized.ab.
39. placebo.ab.
40. drug therapy.fs.
41. randomly.ab.
42. trial.ab.
43. groups.ab.
44. 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43
45. exp animals/ not humans.sh.
46. 44 not 45
47. 24 and 32 and 35 and 46

Table S2. The risk of bias for included studies

Author, Year (Study name)	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other sources of bias
Simon 1999 [37]	Low	Low	Low	Low	Low	Unclear
Silverstein 2000 (CLASS) [20]	Low	Low	Low	Low	Unclear	Unclear
Goldstein 2001 [22]	Low	Unclear	Low	Low	Unclear	Unclear
Sikes 2002 [36]	Unclear	Unclear	Low	Low	Low	Unclear
Hunt 2003 [33]	Unclear	Unclear	Low	Unclear	Unclear	Unclear
Lisse 2003 [35]	Low	Unclear	Low	Low	Unclear	Unclear
Kivitz 2004 [34]	Unclear	Unclear	Low	Low	Unclear	Unclear
Schnitzer 2004 (TARGET) [19]	Low	Low	Low	Low	Unclear	Unclear
Singh 2006 (SUCCESS-I) [5]	Low	Low	Low	Low	Low	Unclear
Laine 2007 (MEDAL) [18]	Low	Low	Low	Low	Low	Unclear
Cheung 2010 [32]	Low	Low	Low	Low	Unclear	Unclear

Table S3. Sensitivity analysis by sample size and risk of bias.

	Study removed from the primary meta-analysis	Included study	Event/Total	RR (95%CI)	Heterogeneity
Sample size					
Concomitant aspirin use - Yes					
Complicated GI events	1	4	152/18340	0.90 [0.65, 1.23]	P = 0.95; I^2 = 0%
Clinical GI events	1	4	340/18340	0.77 [0.62, 0.95]	P = 0.80; I^2 = 0%
Symptomatic ulcer*	-	-	-	-	-
Endoscopic Ulcer**	2	0	-	-	-
Concomitant aspirin use - No					
Complicated GI events	1	4	162/55767	0.34 [0.13, 0.91]	P < 0.001; I^2 = 82%
Clinical GI events	1	4	470/55767	0.50 [0.38, 0.65]	P = 0.40; I^2 = 0%
Symptomatic ulcer*	-	-	-	-	-
Endoscopic Ulcer	1	1	38/615	0.20 [0.11, 0.36]	Not applicable
Risk of bias					
Concomitant aspirin use - Yes					
Complicated GI events	1	4	152/18340	0.90 [0.65, 1.23]	P = 0.95; I^2 = 0%
Clinical GI events	1	4	340/18340	0.77 [0.62, 0.95]	P = 0.80; I^2 = 0%
Symptomatic ulcer*	-	-	-	-	-
Endoscopic Ulcer***	2	0	-	-	-
Concomitant aspirin use - No					
Complicated GI events	1	4	162/55767	0.34 [0.13, 0.91]	P < 0.001; I^2 = 82%
Clinical GI events	1	4	470/55767	0.50 [0.38, 0.65]	P = 0.40; I^2 = 0%
Symptomatic ulcer*	-	-	-	-	-
Endoscopic Ulcer***	2	0	-	-	-

RR: relative risk; CI: confidence interval; GI: gastrointestinal.

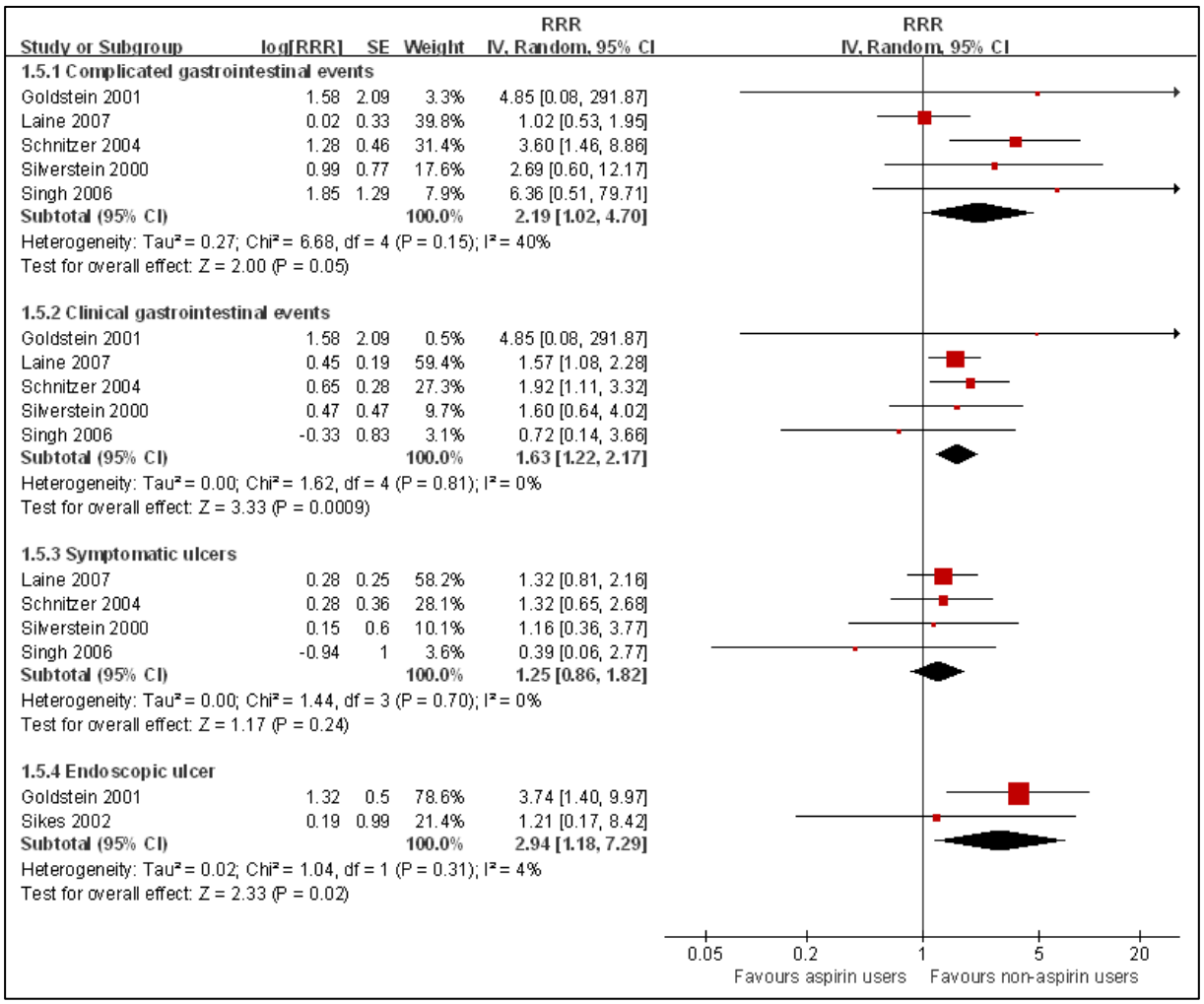
Sensitivity analyses according to sample size excluded the studies with <400 participants. Sensitivity analyses according to risk of bias excluded the studies with high risk of bias on one or more domain, or with unclear risk of bias on three or more domains.

* No study was excluded according to our pre-specified sensitivity analysis criteria.

**The sample size was less than 400 in both of the two studies included in the main analysis, so both were removed.

***There were three domains at unclear risk of bias according to Cochrane handbook for both of the two studies, so both were removed.

Figure S1. Meta-analysis evaluating the interaction of low-dose aspirin use and the gastrointestinal benefit of coxibs over traditional NSAIDs.



RRR: ratio of relative risk.

Note: only those studies with subgroup analysis according to concurrent use of low-dose aspirin were combined. For each included study, the RRR indicated the ratio of the relative risk in the subgroup of low-dose aspirin users and that in the nonusers. An RRR > 1 indicated that the protective effect of coxibs versus traditional NSAIDs is lager in non-aspirin users than in low-dose aspirin users